In the Claims

This listing of claims will replace all previous versions and listings of claims in the application:

1. (Original) A process for controlling the amount of sialic acid present on an oligosaccharide side chain of a glycoprotein produced by mammalian cell culture which comprises:
culturing the mammalian host cell in a production phase of the culture which is characterized by;
   i) adding an alkanoic acid or a salt thereof to the cell culture at a concentration of about 0.1 mM to about 20 mM; and
   ii) maintaining the osmolality of the cell culture at about 250 to about 600 mOsm.

2. (Original) The process according to claim 1 wherein the amount of sialic acid present on the oligosaccharide side chain of the glycoprotein is increased and wherein;
cell specific productivity of the cell culture is decreased by culturing the host cell at a concentration of the alkanoic acid or salt thereof of about 0.1 to about 6mM and maintaining the osmolality at about 300-450 mOsm.

3. (Original) The process of claim 2 in which the host cell is a CHO cell.

4. (Original) The process according to claim 3 wherein the alkanoic acid or salt thereof is sodium butyrate.

5. (Original) The process according to claim 4 wherein the glycoprotein produced is a mammalian glycoprotein.

6. (Original) The process according to claim 5 wherein the glycoprotein is a tumor necrosis factor receptor-immunoglobulin chimera.

7. (Original) The process of claim 6 in which the host cell is a dp12.CHO cell line transfected with the vector carrying the cDNA encoding a soluble type 1 tumor necrosis factor immunoglobulin G_1 chimera.

8. (Original) The process according to claim 1 wherein the amount of sialic cid present on the oligosaccharide side chain of the glycoprotein is decreased and wherein; cell specific productivity of the cell culture is increased by culturing the host cell at a concentration of about 6mM to about 12 mM of the alkanoic acid or salt thereof and maintaining the osmolality at about 450-600 mOsm.

9. (Original) The process of claim 8 in which the host cell is a CHO cell.

10. (Original) The process according to claim 9 wherein the alkanoic acid or salt thereof is sodium butyrate.

11. (Original) The process according to claim 10 wherein the glycoprotein produced is a mammalian glycoprotein.

12. (Original) The process according to claim 11 wherein the glycoprotein is a tumor necrosis factor receptor-immunoglobulin chimera.

13. (Original) The process of claim 14 in which the host cell is a dp12.CHO cell line cell transfected with the vector carrying the cDNA for a soluble type 1 tumor necrosis factor immunoglobulin G_1 TNFR1-IgG_1 chimera.

14. (Original) A process for producing a tumor necrosis factor receptor-immunoglobulin TNFR1-IgG_1 chimeric protein comprising;

(a) culturing a mammalian host cell which expresses a TNFR-IG chimera in a growth phase under such conditions and for a period of time such that maximum cell growth is achieved;

(b) culturing the host cell in a production phase in the presence of sodium butyrate at a concentration of bout 6mM to about 12 mM;

(c) maintaining the osmolality of the production phase at about 450-600 mOsm.

15. (Original) A process for producing a tumor necrosis factor receptor-immunoglobulin TNFR1-IgG_1 chimeric protein comprising;

(a) culturing a mammalian host cell which expresses a TNFR-IG chimera in a growth phase under such conditions and for a period of time such that maximum cell growth is achieved;

(b) culturing the host cell in a production phase in the presence of sodium butyrate at a concentration of about 1mM to about 6 mM;

(c) maintaining the osmolality of the production phase at about 300-450 mOsm.

16. (Original) The process of claim 15 in which the host cell is a CHO cell.

17. (Original) The process of claim 16 in which the host cell is a dp12.CHO line.

18. (Original) A preparation comprising the TNFR1-IgG_1 produced by the process of claim 17.

19. (Original) A therapeutic composition comprising the TNFR1-IgG_1 produced by the process of claim 15, and a pharmaceutically acceptable excipient.

20. (Currently amended) A ~~TNFR1-IgG1~~ human TNFR1-IgG_1 preparation comprising ~~TNFR1-IgG1~~ human TNFR1-IgG_1 molecules wherein the ~~TNFR1-IgG1~~ TNFR1-IgG_1 molecules have a molar ratio of sialic acid to protein of about 4-7.

21. (Currently amended) A ~~TNFR1-IgG1~~ TNFR1-IgG_1 preparation comprising ~~TNFR1-IgG1~~ TNFR1-IgG_1 molecules wherein the ~~TNFR1-IgG1~~ TNFR1-IgG_1 molecules have about 1-2 moles of exposed N-acetylglucosamine residues per mole of ~~TNFR1-IgG~~ TNFR1-IgG_1 protein.

22. (Currently amended) A ~~TNFR1-IgG1~~ TNFR1-IgG_1 preparation comprising ~~TNFR1-IgG1~~ TNFR1-IgG_1 molecules wherein the ~~TNFR1-IgG1~~ TNFR1-IgG_1 molecules have a molar ratio of sialic acid to N-acetylglucosamine of about 0.35 to about 0.5.

23. (Currently amended) The ~~TNFR1-IgG1~~ TNFR1-IgG_1 preparation of claim 22 wherein the molar ration of sialic acid to N-acetylglucosamine is about 0.39 to about 0.45.